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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,928	05/09/2005	Ralph Patrick Braun	HO-P03173US0	6804
29053 7590 11/15/2007 FULBRIGHT & JAWORSKI L.L.P 2200 ROSS AVENUE SUITE 2800 DALLAS, TX 75201-2784			EXAMINER POPA, ILEANA	
			ART UNIT 1633	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/507,928	Applicant(s) BRAUN ET AL.	
	Examiner Ileana Popa	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26 and 28-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26 and 28-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of the invention of Group III, drawn to a method of enhancing the immune response and of species of Gag (p17, p24) codon optimized RT codon optimized Nef truncate, in the reply filed on 08/31/2007 is acknowledged. Upon further consideration, the species election is hereby withdrawn.

Claims 1-25 and 27 have been cancelled. Claims 28-49 are new.

Claims 26 and 28-49 are pending and under examination.

Specification

2. The disclosure is objected to because of the following informalities: Applicant claims priority to PCT/GB03/01213, Application NOs. 10/102,622, and 60/366,058). It is noted that the cross-reference to the above applications is missing from the disclosure.

Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 26, 28-34, 37-39, and 40-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 9-15 of copending Application No. 10/380,981, in view of Kotsopoulou et al. (J Virol, 2000, 74: 4839-4952).

This is a provisional obviousness-type double patenting rejection.

The instant claims are drawn to a method of enhancing an immune response generated by a nucleic acid vaccine by administering an imidazoquinoline amine topically or transdermally 12 to 36 h after the nucleic acid vaccine is administered, wherein the nucleic acid vaccine comprises a nucleotide sequence encoding for HIV-1 Gag or fragments thereof and Nef (claims 26, 28, 37, and 42). The imidazoquinoline amine is imiquimod, i.e., 1-(2-methylpropyl)-1H-imidazo[4,3-c]quinolin-4-amine (see attached drawing) (claim 29), the vaccine can be administered topically or transdermally using a needleless syringe, and the vaccine or the compound is coated on the particles (claims 31-34). The Gag protein contains p17 and p24 (claims 38 and 39) and it is codon optimized (claims 40 and 41).

The application claims are drawn to: (i) a vaccine composition comprising 1-(2-methylpropyl)-1H-imidazo[4,3-c]quinolin-4-amine as adjuvant and a nucleic acid immunogen, wherein the vaccine composition is administered topically or intradermally (claims 1, 2, 9, and 10) and wherein administration of both antigen and adjuvant can be mediated by particles (claims 11 and 12), and (ii) a method of increasing an immune response to an antigen by using the vaccine-composition above, wherein adjuvant

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administration takes place between 7 days prior and 7 days after antigen administration, range that includes the 12 to 36 hours after antigen administration as recited in the instant claim 1 (claims 13-15). The specification defines that the nucleic acid immunogen encodes Gag (which necessarily includes p17 and p24) and Nef (p. 6, lines 1-5 and 23-25, p. 16, lines 20-23).

The application claims do not recite a codon optimized Gag, as required by the instant claims 40 and 41. However, this limitation is not innovative over the prior art. For example, Kotsopoulou et al. teach codon optimized Gag, wherein the codon optimized Gag resemble the codon usage in highly expressed human genes, to improve Gag expression (Abstract, p. 4850, column 1, first full paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the application method by using codon optimized Gag, with a reasonable expectation of success. The motivation to do so is provided by Kotsopoulou et al., who teach that codon optimization leads to increased antigen expression and that such optimized proteins can be used in vaccines (p. 4848, column 2, second full paragraph, p. 4849, column 2 bridging p. 4850).

Thus, the application claims 1, 2, and 9-15 anticipate the instant claims 26, 28-34, 37-39, and 40-42. Since the claims of the Application No. 10/380,981 embrace all limitations of the instant claims, the application claims and the instant claims are obvious variants of one another.

5. Claims 26, 28-43 are provisionally rejected on the ground of nonstatutory

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obviousness-type double patenting as being unpatentable over claims 1-5 and 7-11 of copending Application No. 10/508,143, in view of each Woodberry et al. (J Virol, 1999, 73: 5320-5325) and Kotsopoulou et al. (J Virol, 2000, 74: 4839-4952).

The instant claims are drawn to a method of enhancing an immune response generated by a nucleic acid vaccine by administering an imidazoquinoline amine topically or transdermally 12 to 36 h after the nucleic acid vaccine is administered, wherein the nucleic acid vaccine comprises a nucleotide sequence encoding HIV-1 Gag and Nef or fragments thereof or encoding Gag/RT/Nef truncate (claims 26, 28, 37, 42, and 43). The imidazoquinoline amine is imiquimod, i.e., 1-(2-methylpropyl)-1H-imidazo[4,3-c]quinolin-4-amine (see attached drawing) (claim 29), the vaccine can be administered topically or transdermally using a needleless syringe, the vaccine or the compound is coated on the particles (claims 31-34), the imidazoquinoline amine is administered in the form of a cream (claim 35), and the nucleic acid administration is repeated to provide a primer and booster administration (claim 36). The Gag protein contains p17 and p24 (claims 38 and 39) and it is codon optimized (claims 40 and 41).

The application claims recite to a method of enhancing an immune response generated by a nucleic acid vaccine by administering an imidazoquinoline amine topically or transdermally 12 to 36 h after the nucleic acid vaccine is administered, wherein the nucleic acid vaccine comprises a nucleotide sequence encoding a viral antigen (claims 1-3 and 11). The imidazoquinoline amine is imiquimod, i.e., 1-(2-methylpropyl)-1H-imidazo[4,3-c]quinolin-4-amine (see attached drawing) (claim 29), the vaccine can be administered topically or transdermally using a needleless syringe, the

vaccine or the compound is coated on the particles (claims 4, 5, 7, and 8), the imidazoquinoline amine is administered in the form of a cream (claim 9), and the nucleic acid administration is repeated to provide a primer and booster administration (claim 10).

Although the specification defines that the nucleic acid could encode Gag (i.e., comprising p17 and p24), Nef or Pol, the specification does not teach a fusion between Gag and Nef or between Gag, RT, and Nef truncate, as recited in the instant claims 26, 37. However, this is not innovative over the prior art, which teaches the necessity of using polyepitope DNA vaccines comprising Gag, Pol, and Nef epitopes for vaccination against HIV-1, wherein the Pol epitopes are derived from RT (see for example Woodberry et al. (Abstract, p. 5320, columns 1 and 2, p. 5321, Table I). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the application method according to the teachings of Woodberry et al., with a reasonable expectation of success. The motivation to do so is provided by Woodberry et al., who teach that polyepitope vaccines can preempt the formation of CTL-escape HIV-1 mutants (Abstract, p. 5320, columns 1 and 2).

The application claims do not recite a codon optimized Gag, as required by the instant claims 40 and 41. However, this limitation is not innovative over the prior art. For example, Kotsopoulou et al. teach codon optimized Gag, wherein the codon optimized Gag resemble the codon usage in highly expressed human genes, to improve Gag expression (Abstract, p. 4850, column 1, first full paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the

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application method by using codon optimized Gag, with a reasonable expectation of success. The motivation to do so is provided by Kotsopoulou et al., who teach that codon optimization leads to increased antigen expression and that such optimized proteins can be used in vaccines (p. 4848, column 2, second full paragraph, p. 4849, column 2 bridging p. 4850).

Thus, the application claims 1-5 and 7-11 anticipate the instant claims 26, 28-42. Since the claims of the Application No. 10/508,143 embrace all limitations of the instant claims, the application claims and the instant claims are obvious variants of one another.

6. In addition to the above, Applicant is required to disclose any additional application or patents that would be material for the patentability of this application.

It is noted that Applicant is inventor on a number of applications directed to using imidazoquinoline amine in a method of enhancing the immune response to DNA vaccines.

Claim Rejections - 35 USC § 112, 2nd paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

8. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26 and 45 reciting a heterologous promoter comprising exon 1 are indefinite because it is unclear what exon 1 is claimed. While the specification defines that the HCMV IE promoter can include CMV exon 1, the claims are broader than this and are practically drawn to any first exon derived from any gene. By reading the claim, one of skill in the art would not be able to determine what exon is claimed. Therefore, the metes and bounds of the claims cannot be determined and the claims are indefinite.

Amending the claims to recite a HCMV promoter containing the first exon of the IE-1 gene or amending claim 45 to recite the first exon of the IE-1 and to depend from claim 44 would obviate this rejection.

For examination purposes, the claims will be interpreted as being drawn to a HCMV promoter containing the first exon of the IE-1 gene.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 26, 28, 29, 36-38, 42, and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodberry et al. (J Virol, 1999, 73: 5320-5325), in view of each Peter et al. (Vaccine, 2001:19: 4121-4129, Abstract), Goulder et al. (Immunol Lett, 2001, 79: 109-116, Abstract), and Miller et al. (WO 93/20847).

Woodberry et al. teach a method of inducing an immune response generated by a polyepitope DNA vaccine comprising a nucleic acid encoding HIV Nef-Pol-Gag-Nef-Pol-gp120-Nef (claims 26, 37, 38, and 42), wherein the vaccine is administered as a primer and as a booster (claim 36), and wherein the nucleic acid encodes a fusion protein comprising the epitopes (claim 49) (Abstract, p. 5320, columns 1 and 2, p. 5321, columns 1 and 2, Fig. 1, and Table I). The Gag epitope is from p17 (see Abstract in Goulder et al. and Table 1 in Woodberry et al.), the Pol epitope is from RT (see Abstract in Peter et al. and Table 1 in Woodberry et al.), and the Nef epitopes are Nef 180-189 and 190-198 (i.e., Nef truncate, according to the definition in the specification on p. 38, lines 23 and 24). Therefore, the polyepitope vaccine of Woodberry et al. encodes Nef-RT-Gag (claims 47 and 48).

Woodberry et al. taken with Peter et al. and Goulder et al. do not teach using imiquimod as adjuvant (claims 26, 28, and 29). Miller et al. teach using imidazoquinoline amines such as imiquimod as a vaccine adjuvant to enhance both humoral and cellular immune responses (p. 3, lines 34-37, p. 4, lines 4-9, p. 5, lines 6-20, p. 12, lines 28-30, p. 13, lines 27-32). Miller et al. also teach topical imiquimod administration 48h after vaccine administration (claim 26) (p. 28, lines 1-12). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Woodberry et al., Peter et al. and Goulder et al. by using imiquimod as an adjuvant, with a reasonable expectation of success. The motivation to do so is provided by Miller et al., who teach imiquimod as a universal adjuvant capable to enhance the immune responses elicited by a variety of antigens (p. 13, lines 27-37, p.

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14, lines 1-27). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that imiquimod can be successfully used to enhance the immune response to vaccines. Although Miller et al. teach administering imiquimod after the vaccine administration (i.e., 48 hours), they do not specifically teach 12 to 36 hours (claim 26). However, it would have been obvious to the ordinary skilled artisan to vary the parameters in the method with the purpose of optimizing the results. Absent evidence of unexpected results, it is generally not inventive to discover the optimal working conditions of a prior art method, such conditions can be identified by routine experimentation. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

11. Claims 26, 28, 29, 36-43, and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al., in further view of both Zhang et al. (Immunol Lett, 2001, 79: 93-96) and Kotsopoulou et al. (J Virol, 2000, 74: 4839-4952).

The teachings of Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al. are applied as above for claims 26, 28, 29, 36-38, 42, and 47-49.

Woodberry et al., Peter et al., Goulder et al., and Miller et al. do not teach p24 (claims 39 and 43). Zhang et al. teach that p24 as suitable for HIV vaccines (Abstract, p. 93, column 2, p. 95, columns 1 and 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Woodberry et al. and Peter et al., Goulder et al., and Miller et al. by further including p24, with a reasonable

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expectation of success. The motivation to do so is provided by Zhang et al., who teach p24 as useful for designing HIV vaccines (Abstract, p. 96, columns 1 and 2). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that vaccines containing multiple epitopes can be successfully made and used.

Woodberry et al., Peter et al., Goulder et al., Miller et al., and Zhang et al., do not teach codon optimization (claims 40, 41, and 43). Kotsopoulou et al. teach codon optimized Gag and Pol, wherein the codon optimized Gag and Pol resemble the codon usage in highly expressed human genes, to improve Gag and Pol expression (Abstract, p. 4850, column 1, first full paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method Woodberry et al., Peter et al., Goulder et al., Miller et al., and Zhang et al. by using codon optimized Gag and RT with a reasonable expectation of success. The motivation to do so is provided by Kotsopoulou et al., who teach that codon optimization leads to increased antigen expression and that such optimized proteins can be used in vaccines (p. 4848, column 2, second full paragraph, p. 4849, column 2 bridging p. 4850). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that proteins can be successfully optimized with respect to codon utilization. The limitation of the vaccine being a plasmid (claim 46) is not innovative over the prior art, which teaches the use plasmids as vaccines (see Kotsopoulou et al., p. 4840, column 1, fourth full paragraph).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

12. Claims 26, 28-35, 36-38, 42, and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al., in further view of both Fynan et al. (Proc Natl Acad Sci USA, 1993, 90: 11478-11482) and Spruance et al. (The journal of Infectious Disease, 2001, 184: 196-200; Applicant's IDS).

The teachings of Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al. are applied as above for claims 26, 28, 29, 36-38, 42, and 47-49. Woodberry et al., Peter et al., Goulder et al., and Miller et al. do not teach administration of the vaccine or compound with a needleless syringe, wherein the vaccine or the compound are coated on particles and wherein the vaccine is transdermally delivered (claims 30-34). Fynan et al. teach the use of a gene gun (i.e., needleless syringe) to transdermally deliver DNA vaccines in the form of vaccine-coated gold beads (Abstract, p. 11480, column 1 bridging column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to deliver the vaccine of Woodberry et al., Peter et al., Goulder et al., and Miller et al. by using the gene gun of Fynan et al., with a reasonable expectation of success. The motivation to do so is provided by Fynan et al., who teach gene gun as the most efficient method of immunization (p. 11480, column 1, last paragraph). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches the successful use of

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gene guns to administer DNA vaccines. The limitation recited in claim 35 is not innovative over the prior art, which teaches that imidazoquinoline amines can be topically administered in the form of a gel (see Spruance et al. Abstract, p. 196, column 2, first full paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to substitute the gel of Spruance et al. with a cream to achieve the predictable result of transdermally delivery of the compound (see *KSR International Co. v. Teleflex Inc.*, 550 U.S., 82 USPQ2d 1385, 2007). Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

13. Claims 26, 28, 29, 36-38, 42, 44, 45, and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al., in further view of Mikkelsen et al. (Transgenic Research, 1992, 1: 164-169).

The teachings of Woodberry et al. taken with Peter et al., Goulder et al., and Miller et al. are applied as above for claims 26, 28, 29, 36-38, 42, and 47-49.

Woodberry et al., Peter et al., Goulder et al., and Miller et al. do not teach HCMV IE containing the first promoter of the IE-1 gene (HCMV IE-1) (claims 44 and 45).

Mikkelsen et al. teach the use of HCMV IE-1 to drive gene expression, wherein HCMV IE-1 is active in a variety of cells (p. 164, column 1p. 167, columns 1 and 2). It would have been obvious to one of skill in the art, at the time the invention was made, to substitute the promoter of Woodberry et al., Peter et al., Goulder et al., and Miller et al. for the promoter of Mikkelsen et al. to achieve the predictable result of expressing the

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DNA in the transfected cells (see *KSR International Co. v. Teleflex Inc.*, 550 U.S., 82 USPQ2d 1385, 2007). Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

14. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER

4/12/07